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Dr. WILLIAM ALLEN MILLER, Treasurer and Vice-President, in the Chair.

"On the ultimate Nerve-fibres distributed to Muscle and some other Tissues, with observations upon the Structure and probable Mode of Action of a Nervous Mechanism"*. Being the CROONIAN LECTURE for 1865, delivered by LIONEL S. BEALE, M.B., F.R.S., Fellow of the Royal College of Physicians, Professor of Physiology and of General and Morbid Anatomy in King's College, London; Physician to King's College Hospital.

It seems to have been the desire of the founder of the lectureship which I have the honour to hold this year, that a lecture or discourse on the nature or property of local motion, accompanied by an experiment, should

* This Lecture will be published shortly in a separate form, with all the drawings. The references made in the text to illustrations apply to the drawings and diagrams exhibited during the delivery of the Lecture.

be delivered annually to the Fellows of the Royal Society. It appears that the subject of muscular motion was selected by many of the earlier Croonian lecturers, and it has been generally considered that the Croonian Lecture should be confined to this department of local motion. Although this view was founded upon a misconception, it would indeed have been difficult to have selected a subject better adapted for frequent and repeated investigation and illustration than muscular motion. Notwithstanding more than a century has elapsed since the first Croonian Lecture was delivered, the nature of muscular motion, and the mechanism taking part in its production, still remain to be discovered. In this as in every other department of natural knowledge, it is to be noticed that the gradual progress made by the unremitting labour of successive observers, so far from exhausting the fields of scientific inquiry, seems but to prepare the way for ever-increasing advance.

By the excellent custom of appointing lecturers to deliver at certain intervals of time lectures upon the same department of natural knowledge, the actual progress achieved from time to time may be distinctly defined and duly registered, and new lines of inquiry suggested for future investigators in the same department. Although I have been led to choose for the subject of my lecture an anatomical question which seems extremely simple and of limited extent, I am compelled to leave many points but imperfectly studied; and notwithstanding I have worked at this question earnestly for several years, my conclusions are in many respects still incomplete.

It is remarkable how the positive determination of a simple question of fact may, as it were, recede as the investigation advances. However minute the detail, more and ever more detail seems required before all doubt can be removed from the mind of the student.

I should not have ventured to ask the attention of the Fellows of the Royal Society to minute and, necessarily, in many respects incomplete anatomical detail, were it not that some broad questions of very general interest are involved in the inquiry I have undertaken; and I think that I shall render what I have to say far less tedious and irksome than it would otherwise be, if I state, in the first instance, the questions proposed for discussion, and the general nature of the inferences I have arrived at.

It seems to me that we can scarcely hope to determine the manner in which the nervous system influences the muscular and other tissues, until we have ascertained how the ultimate branches of nerve-fibres are arranged, and have demonstrated by actual observation, or proved by other means, whether the nerves are disposed so as to form loops or plexuses, or whether they exhibit distinct ends, or terminate in special organs or by becoming continuous with other tissues. And it is impossible to separate from this inquiry the further and wider question, concerning the necessary structure and typical arrangement of a nervous apparatus.

Our view regarding the nature of the force which produces such marvellous phenomena as those known to result from nervous action, will be materially influenced by the conclusion which we are led to accept regarding the fundamental arrangement of the nerve-cells and fibres, central and peripheral.

If it could be shown that a nerve passes from its centre and ends by free terminations, or by becoming continuous with the muscular tissue, we should scarcely adopt the same general conclusion regarding the manner in which the nerve-centre influences the contractile tissue as we should if it were shown that the nerve merely passed amongst the muscular fibres without being necessarily even in actual contact with them, and returned towards, and eventually became connected with, the nerve-centre, without there being any solution of continuity in any part of the circuit. The investigations recorded in this and other memoirs have led me to conclude that nerves invariably form circuits, and that there are in truth no ends at all. I believe that the nerve machinery is a complete circuit, and that the active phenomena are due rather to an alteration in the intensity of the current passing along the nerves, than to its sudden interruption and completion.

In this Lecture I hope to be able to adduce facts which indicate the existence of fibres passing from and towards all central and peripheral nerve-cells.

Before I proceed to the special subject of my Lecture, I must offer a few remarks upon *contractility*. Of late this term has been applied to movements occurring in living organisms which seem to me to be quite distinct in their essential nature from contractility. I cannot hold that the movements occurring in an amœba or white blood-corpuscle are of the same nature as those which occur in muscle, and I cannot, therefore, regard both classes of movements as manifestations of one property, *contractility*.

Of the Movements occurring in Cells and in the Tissues of Living Beings, and on Contractility.

Vital movements.—The peculiar movements occurring in a mass of germinal matter are illustrated by the drawing now exhibited. Protrusions may occur at one or many points of the mass at the same time, and the whole mass may move in one direction like an amœba. Now it will scarcely be maintained by any one that the changes of form occurring in a mass of living matter are due to external agency. As far as can be ascertained by observation, the movement is primary, and depends upon the active forces inherent in the matter itself. This form of motion has never been explained or accounted for; but as it ceases with the death of living matter, it is only reasonable to infer that it is intimately associated with those other phenomena which are peculiar to matter in the living state. It may therefore be termed *vital motion*, to distinguish it from every other kind of movement known. The rotation and other movements affecting the "pro-

toplasm" of certain vegetable cells, and the motion of masses of germinal matter in various tissues of man and animals must be included in this class of vital movements*.

Ciliary action is, I think, a secondary phenomenon, due to changes going on within the cell, but probably very intimately connected with the currents flowing to and from the germinal or living matter, and the altered tension thus caused in the cell. Ciliary motion is not dependent upon nervous action, nor is it due to any disturbance in the surrounding medium. Ciliary motion cannot be regarded as a *vital* movement, although it is probably due to changes which are consequent upon vital phenomena. Cilia consist of "formed material."

* No one will be more ready to receive and acknowledge that these movements and other phenomena characteristic of living matter are due to ordinary force than myself, so soon as the correctness of such a doctrine shall have been proved, or, indeed, any advance towards this end shall have been made; but as a working physiologist desiring to see, and promote to the utmost, real advance in this department of science, I consider it a duty to oppose as strongly as I can the practice pursued by some scientific authorities in the present day, and especially in this country, of reiterating the assertion that all the phenomena of living beings are to be accounted for by the action of ordinary force. Nothing can retard true progress more than exaggerated statements with reference to advance in any special direction. It is almost certain that the manifest anxiety to substitute for quiet proof intense and positive language, merely indicates bias, if not prejudice, in favour of views not supported by facts. I have already stated, not only that the doctrine does not rest upon any sound evidence whatever, but have drawn attention to the phenomena which occur in the simplest form of living matter, which never have been, and which I believe cannot be explained upon any known physical or chemical laws. Instead of these objections being answered, or the challenge to consider the matter in detail being accepted, we are told that the "tendency of modern science is towards this" apparently much-desired "end, and that although living matter cannot yet be prepared by man, the day is not far distant when its artificial production will be rendered possible," and so forth!

The fallacy underlying many of the modern doctrines is obscured, if not entirely concealed, by the very ingenious choice of words. For instance, when it is stated, with what appears to be learned precision, that force is "conditioned" by the "*molecular machinery*" existing in the cell, few probably would be led to inquire what the molecular machinery was, and how the "conditioning" took place. Now it so happens that the changes in question occur without the existence of anything to which the term machinery can be properly applied. Instead of the living cell being like a machine, it is perhaps less like a machine than anything else that we have any knowledge of. The "living machine" is just a very minute mass of soft, colourless, transparent, semifluid matter, endowed with very wonderful properties or powers, in which matter is decomposed and its elements rearranged, while its forces are conditioned in a manner that cannot be effected by man with the aid of the most perfect machinery and elaborate apparatus his ingenuity has devised. Living matter is not a machine, nor does it act upon the principles of a machine, nor is force conditioned in it as it is in a machine, nor have the movements occurring in it been explained by physics, or the changes which take place in its composition by chemistry. The phenomena occurring in living matter are peculiar, differing from any other known phenomena; and therefore, until we can explain them, they may be well distinguished by the term *vital*. Not the slightest step has yet been made towards the production of matter possessing the properties which distinguish living matter from matter in every other known state.

In the immediate vicinity of ciliated cells are sometimes observed cells with open mouths, out of which mucus and various substances, formed or secreted in the interior of the cell, pass. In the formation of these products, nutrient matter from the blood, after passing through the attached extremity of the cell, is probably absorbed by the living matter. At the same time the outermost portion of the latter becomes converted into the peculiar contents of the cell, and thus the formed matter which has been already produced becomes pushed towards the orifice. This is explained by the drawing; and I think that the movements of cilia are brought about by a somewhat similar series of changes, in which the germinal or living matter, usually termed "nucleus," plays the active and most important part.

Movements of granules within cells.—The movement of insoluble particles from one part of a cell to another, as occurs in the radiating pigment-cells of Batrachia, is probably due to alteration in the direction of the flow of fluid in the cells, *from* the cavity of the cell *towards* the tissues, or *from* the surrounding tissue *into* the cell. If the capillaries were fully distended, fluid would permeate their walls and would pass into the cavity of the cells, in which case the insoluble particles would gradually become diffused and would pass into all parts of the cell; while, on the other hand, if the capillaries were reduced in diameter, and the lateral pressure upon their walls reduced, there would be, as is well known, a tendency for the fluid in the surrounding tissue to flow towards the vessels and pass into their interior. In this case the quantity of fluid in the cells would be gradually reduced, and the insoluble particles would become aggregated together and would collect in those situations where there was most space, as in the central part of the cell, around the nucleus. Moreover, in the last case, the flow of fluid, which constantly sets towards the nucleus, would be instrumental in drawing the particles in this same direction, while if the cell contained a considerable proportion of fluid, the currents would pass between the particles without moving them. Evaporation, as it occurs after death, causes concentration of the insoluble particles towards the centre of the cells.

On the other hand, the changes in the pigment-cells of the frog have been considered by Professor Lister to be due to *vital actions,* and he agrees with Wittich and others that they are under the immediate control of the nervous system. Indirectly of course they are, but I do not think that any experiments have proved satisfactorily that the nerves exert any *direct* influence upon the movements of the particles in these cells. It is well known that the nerves govern the calibre of the vessels, and thus influence the amount of fluid in the surrounding tissue, and in this indirect manner they doubtless affect the movements of the particles in the cells. The reader will find a full account of Prof. Lister's experiments, and the arguments deduced from them, in his paper "On the Cutaneous Pigmentary System of the Frog," published in the Philosophical Transactions for 1858.

Muscular movement is illustrated by the figures to which I now refer,

and which are intended to show the alterations in form supposed to take place in the ultimate particles of any contractile tissue—movements occurring in definite directions, which may be represented by lines at right angles to one another. These movements are quite distinct from those varied movements in all directions which affect matter in the germinal or living state. Contractile tissue is formed material, and contractility occurs in tissue which does not exhibit any of those properties or powers which distinguish living matter. It seems to me, therefore, that contractility is not a *vital property*; and I think that the term *contractility* should be restricted to movements which are remarkable for their constant repetition, and for the simplicity of their character. The changes which occur in the particles of a muscle during action might be spoken of as alternate *shortening* and *lengthening*.

Experiment.

The phenomena of contractility can be studied more satisfactorily in the muscles of the common maggot or larva of the blow-fly than in those of any other animal I am acquainted with. The movements, which are very beautiful, continue for ten minutes or a quarter of an hour after the muscles have been removed from the body of the recently killed animal; and I hope to be able to prepare a specimen which can be passed round in one of the portable microscopes and examined by the Fellows. [Preparation sent round.] In the winter I have seen the contractions continue for upwards of half an hour. But the most beautiful and instructive method of examination is under the influence of polarized light, with a plate of selenite. In the microscope upon the table, the arrangement has been made; and when the ground is green, the waves of contraction which pass along each muscular fibre in various directions, are of a bright purple. In other parts of the field the complementary colours are reversed. There are few microscopic objects, that I am acquainted with, so beautiful as this. With the aid of very high powers, the actual change occurring in the contractile tissue as it passes from a state of relaxation to contraction, and from this to relaxation again, may be studied, and for many minutes at a time*.

Molecular movements.—The cause of the so-called molecular movements is probably complex, but quite independent upon any phenomena peculiar to living beings.

The various movements occurring in the ultimate elementary parts or "cells" of living beings may be arranged as follows:—

1. *Primary or vital movements.*—Affecting matter in the living state only and occurring in every direction, as seen in the amœba, white blood-corpuscle, mucus- and pus-corpuscle, young cells of epithelium, and in germinal matter generally.

* The character of muscular movements is fully described in Mr. Bowman's well-known paper (Phil. Trans. 1841). See also Mr. Bowman's article, "Muscular Motion," in Todd's Cyclopædia of Anatomy and Physiology.

2. *Secondary movements*—the consequence of vital movements, or of other phenomena, affecting matter which is not in a living state:—

a. *Ciliary movements.*—Probably due to alterations in the quantity of fluid within the cell, the changes in the proportion of fluid being brought about by the action of the living or germinal matter in the cell.

b. *Movements of solid particles suspended in fluid in cells, caused by currents in the fluid*, as the pigmentary matter in the pigment-cells of the frog.—Due to the motion of the fluid as it passes into or out of the cell through its permeable wall, this movement being dependent upon changes taking place external to the cell.

c. *Molecular movements.*—Which affect all insoluble particles, in a very minute state of division when suspended in a fluid not viscid.

d. *Muscular movements.*—Due to a disturbance (electrical or otherwise) in the neighbourhood of a contractile tissue—that is, a structure so disposed that its constituent particles are susceptible of certain temporary alterations in position, which alterations take place in certain definite directions only.

Distribution of Nerves to Involuntary Muscle.

Distribution of nerves to the muscular fibres and other tissues in the bladder of the frog.

The demonstration of the ultimate arrangement of the most minute nerve-fibres is a matter of such great difficulty that the anatomist is compelled to search with the utmost care for a texture the natural structure of which happens to be favourable for his investigation. There are very few textures which possess so many advantages as the bladder of the frog. It is so thin and transparent, that it may be regarded as a natural dissection and thinning-out of some of the most delicate tissues. The unstriped muscular fibres of this organ are extremely fine, and are slightly separated from one another. Nerve-fibres can often be seen in the intervals between the fibres.

I have therefore selected this for illustrating the ultimate ramification of the nerve-fibres in involuntary muscle; but I believe the statements which I shall make will be found to apply with equal force to every variety of this particular form of muscular tissue.

With regard to the presence of nerve-fibres in involuntary muscle, I may remark that nerve-fibres have been demonstrated in so many different cases, that it is more in accordance with the positive knowledge already gained to infer that they exist in relation with every form of contractile tissue, even in cases in which we may still fail to demonstrate them, than to infer they are absent simply because we have failed to render them distinct*.

* By contractile tissue I mean a tissue in which simple movements like shortening and lengthening alternate with one another, each movement being a mere repetition of the first movement that occurred when the *formation* of the contractile tissue was complete.

The bundles of dark-bordered fibres which may be traced to the posterior part of the frog's bladder divide and subdivide freely, spreading out in the form of a lax network, the fibres constituting which may be followed for some distance, and many may be traced to their ultimate distribution in the thin tissue of the bladder. Over a great part of the frog's bladder, however, no dark-bordered fibres or bundles of moderately coarse fibres can be detected; yet the organ is in every part very freely supplied with nerves.

Bundles of excessively fine fibres, first described by me*, may be traced running parallel with many of the small arteries, and may be seen to divide and subdivide into finer bundles, which at length form a plexiform network. Here and there is seen a plexus of very fine fibres, from which bundles of fine fibres diverge in different directions. That very many of these fine fibres come from the numerous ganglion-cells found in connexion with the nerve-trunks there is no doubt; and it is equally certain that many also result from the division and subdivision of dark-bordered fibres. But whether the large dark-bordered fibres seen in the nerve-trunks pass directly to their distribution in the bladder, or in the first place become connected with ganglion-cells, it is difficult to decide with absolute certainty; I have, however, traced several of the large fibres directly from the trunks to their distribution, but even in these instances I am not prepared to assert that no branches pass to the ganglion-cells. My impression is that sometimes this is the case, but that some of the fibres pass to their distribution without there being any such connexion with ganglion-cells; and I think it probable that, of the fibres resulting from the division of a dark-bordered fibre derived from the cord, some may become connected with ganglion-cells, while others may pass to their distribution in the bladder without being connected with these cells.

In the very thin membrane of which the walls of the frog's bladder are composed we may follow out the distribution of nerves—*a* to the muscular tissue, *b* to the surface of the mucous membrane, *c* to the vessels, and *d* to the connective tissue.

In this drawing the general arrangement of the nerve network is represented, from which fibres pass to supply all the tissues of the bladder.

Upon the external surface of the lung of the frog muscular fibre-cells exist in small number, and to these a network of delicate nerve-fibres is distributed. These muscular and nerve-fibres are, however, much more highly developed upon the newt's lung than upon that of the frog. But in this Lecture I restrict myself to the consideration of the distribution of nerves to the muscular fibre-cells, which is described in very few words and will be at once understood by reference to the diagram to which I now direct attention.

The muscular fibre-cells of the bladder itself and of the small arteries

* "On very fine Nerve-fibres in Fibrous Tissues, and on Trunks composed of very fine Fibres alone" (Archives of Medicine, vol. iv.).

are crossed sometimes in two or three places by very fine nerve-fibres; and not unfrequently the nerve-fibre runs parallel with the muscular fibre-cell for some distance.

These nerve-fibres are extremely fine, and require very high powers for their demonstration. They are certainly not connected in any way either with the nucleus or with the contractile tissue of the muscular fibre. They cross the fibre either obliquely or at right angles; and oftentimes a nerve-fibre runs for some distance parallel with the muscular fibre. The influence, therefore, exerted by the nerve-fibre cannot depend upon any continuity of texture between it and the contractile tissue, but is doubtless due to the passage of a current through the nerve, which determines a temporary alteration in the relations to one another of the particles of which the contractile tissue consists.

Although I speak of the ultimate nerve-fibres as being arranged so as to form a network, it must not be supposed that this network is arranged on the principle of a capillary network. Every fibre of this network is compound; so that perhaps the term "plexus" more truly describes the arrangement. "Plexiform network," I think, expresses the character of the arrangement still more exactly*.

Some have said that my view accords with the old idea of looplike terminations of nerves; and this is in the main true, but the course of one single fibre forming the loop is far more extensive than was supposed by the older observers, and the "looped fibres" divide and subdivide into finer fibres. This diagram is intended to represent a plan of the arrangement which is shown to exist in many tissues according to my observation.

Although it be admitted that networks are formed, it might be said that from them fine fibres may branch off here and there, and *terminate* in ends within the space or area. The results of actual observation and a careful consideration of the various facts bearing upon the question are, however, strongly opposed to such a doctrine.

Distribution of nerves to the muscular fibres in the walls of arteries, veins, the intestine, ducts of glands, &c.

So far as I can ascertain, all involuntary muscular fibre is freely supplied with nerve-fibres, and in all cases the nerves are arranged so as to form networks. In many instances ganglia are seen in connexion with the nerves ramifying amongst the muscular fibre-cells encircling the vessels. I have seen such upon the vessels of all the viscera and those of the palate

* "In using the term network, I do not mean to imply that fine nerve-fibres unite with each other after the manner of capillaries, but merely that the *bundles* of fibres are arranged like networks. The fibres composing the bundles do not anastomose. In lace the appearance of a network of fibres is produced; but every apparent thread is composed of several, each of which pursues a complicated course, and forms but a very small portion of the boundary of any one single space. In Plate XLI. fig. 5, a nervous network exists; but each cord is compound, and composed of numerous fibres which never anastomose."—*Note appended to a paper in the Phil. Trans.* 1862.

of the frog: they are to be detected upon the iliac arteries in considerable number. The results of Mr. Lister's experiments render it probable that ganglia exist in connexion with the arteries of the limbs (Phil. Trans. pt. 2 for 1858, p. 620).

In this figure a small ganglion in course of development upon one of the iliac arteries of the frog is represented; and several fine branches of nerve-fibres can be followed amongst the muscular fibre-cells. I have seen very fine nerve-fibres beneath the circular muscular fibre-cells, apparently lying just external to the lining membrane of the artery, and composed of longitudinal fibres with elongated nuclei—an observation which confirms a statement of Luschka's. I have not succeeded in satisfying myself that nerve-fibres are ever distributed to the lining membrane of an artery, although, from the appearances I have observed, I cannot assert that this is not the case. In the auricle of the heart and at the commencement of the venæ cavæ, very fine nerve-fibres are certainly distributed very near indeed to the internal surface, being separated from the blood only by a very thin layer of transparent tissue (connective tissue).

The distribution of nerve-fibres to the coats of a small artery about the $\frac{1}{800}$th of an inch in diameter is represented in this drawing. In all cases (and I have examined vessels in almost all the tissues of the frog), not only are nerve-fibres distributed in considerable number upon the external surface of the artery, ramifying in the connective tissue, but I have also followed the fibres amongst the circular fibres of the arterial coat. The nerves can be as readily followed in the external coat as in the fibrous tissues generally; and the appearance of the finest nucleated nerve-fibres, already alluded to, enables one to distinguish them most positively from the fibres of the connective tissue in which they ramify.

These nerves invariably form networks with wide meshes. I have demonstrated such an arrangement over and over again. A similar disposition may be seen in the auricle of the frog, in the coats of the venæ cavæ near their origin from the auricle, among the striped muscular fibres of the lymphatic hearts of the posterior extremities of the frog, and in other situations. Kölliker confesses that he has not succeeded in observing distinct *terminations* to the nerves distributed to the vessels of muscles. He states that some arteries are completely destitute of nerves, and, apparently without having given much attention to the subject, says "hence it is evident that the walls of the arteries are not in such essential need of nerves as is usually supposed." It is easy to demonstrate nerves in considerable number on all the arteries of the frog, and in the case of certain vessels of man and the higher animals in which we have failed to demonstrate nerves, it is more reasonable to assume that they are there, although they have not been seen, than to infer their absence simply because we have failed to render them distinct. In the case of the umbilical arteries of the fœtus and their subdivisions in the placenta, it is quite certain there are no true dark-bordered nerve-fibres, but we now know that the active part of a nerve

may consist of an exceedingly delicate, pale, and scarcely visible fibre, connected with a nucleus. Such delicate fibres and nuclei are to be demonstrated amongst the muscular fibres of these arteries, but in consequence of not having been able to trace them continuously for any great distance, I cannot assert that these are true nerves; but no one has yet proved they are not nerves, or has demonstrated their real nature.

The nerves which supply the small arterial branches in the voluntary muscles of the frog, come from the very same fibres which are distributed to the muscles. I have seen a dark-bordered fibre divide into two branches, one of which ramified upon an adjacent vessel, while the other was distributed to the elementary fibres of the muscle. In my paper "On the Structure of the Papillæ of the Frog's Tongue" these statements have been confirmed; and in the figure to which I now point, nerves distributed to arteries and to elementary muscular fibres of striped muscle are seen to be derived from the same trunk of dark-bordered nerve-fibres.

Distribution of Nerves to Striped Muscle.

Of the arrangement of dark-bordered fibres distributed to voluntary muscle and other tissues.

The plexiform arrangement of nerve-trunks and nerve-fibres is one which is very general, and was known even to the older anatomists. It can be demonstrated in many cases even by rough dissection. It exists not only in the case of nerves distributed to muscle, but, as far as is known, to every other tissue which receives a supply of nerves. Many of these networks are very beautiful; and the arrangement is illustrated by these figures, which represent the bundles of dark-bordered nerve-fibres distributed respectively to the diaphragm of the white mouse, the mylohyoid of the green tree-frog, and the eyelid of the same animal. The fibres constituting the bundles never run perfectly parallel with one another, nor can a separate fibre usually be followed for any great distance. This arises from the fact that the fibres frequently cross one another, and many seem to pursue a spiral course. The spiral arrangement of nerve-fibres has been already described in former communications. At an early period of development one fibre may be seen coiled spirally round the other, as is well shown in this drawing*. The rule seems to be universal that fibres on one side of a trunk cross over and pursue their course on the opposite side. Those on the lower part of a trunk soon pass to the upper part, and *vice versâ.* Instead of a nerve passing to its distribution by the shortest route, it invariably seems to pursue a very circuitous course. The course of the nerve-fibres in the optic commissure is not peculiar to this part of the nervous system, but a similar arrangement is to be met with in all nerves. When two trunks meet, as represented in this figure, fibres are found to pursue the several courses represented by the lines.

* See also my paper "On the Structure of the so-called Apolar, Unipolar, and Bipolar Nerve-cells," Phil. Trans. 1863.

Division of the dark-bordered nerve-fibres as they approach their distribution.

It is to be specially noted that the dark-bordered fibres very frequently divide, and, in consequence of the fibres being exceedingly thin at the points of division, which occur, for the most part, just where a bundle of fibres divides into two branches, they are seen only in very carefully prepared specimens. Although Wagner long ago showed that dark-bordered fibres underwent subdivision, the numerous subdivisions which I have demonstrated in all dark-bordered fibres near their peripheral distribution and also as they pass towards the nerve-centre, have not been generally observed. The number of fibres into which a single dark-bordered fibre divides is very great in a comparatively short course. The resulting subdivisions pursue very different directions, and can often be followed for a considerable distance as they run with other dark-bordered fibres. From this it follows that many different parts of a muscle at a distance from one another may be supplied with nerves which result from the subdivision of a single dark-bordered fibre.

The fibres resulting from the subdivision of the dark-bordered fibres are of less diameter than the parent trunks; but the area of the section of two fibres would invariably be much greater than that of the parent trunk. For the most part the fibres divide dichotomously; but sometimes a fibre is seen to divide into as many as three or four divisions, and in muscle five, six, or even more dark-bordered fibres have been seen to result from the division of one. The finer dark-bordered fibres often run in the same bundle with coarse dark-bordered fibres, the former being in fact much nearer to their ultimate destination than the latter. The dark-bordered fibres distributed to the muscles of the frog often divide into two very fine fibres, as represented in several of these figures. These fibres may be traced onwards for some distance. They do not exhibit the dark-bordered character. They appear pale and granular, and connected with them at varying intervals are nuclei. These pale nucleated fibres in the frog are often less than the $\frac{1}{50000}$ of an inch in diameter. They are nevertheless compound, and consist of bundles of still finer fibres. These in fact, although much narrower, correspond to the pale, granular, but nucleated intermuscular nerves first described by me in the muscles of the mouse (Phil. Trans. 1860). The very fine compound fibres still continue to divide and subdivide, and assist to form plexuses and networks in precisely the same manner as the dark-bordered fibres, of which they are the continuation. It is quite certain that these pale fibres are true nerve-fibres, for they are directly continuous with the dark-bordered fibres. Instead of breaking up into one or more bundles of fine fibres, a dark-bordered fibre not unfrequently divides into a finer dark-bordered, and a bundle of fine fibres, as represented in this drawing from the frog's mesentery.

Of the fine fibres running with the dark-bordered fibres.

We find in the same nerve-trunk fine and coarse dark-bordered fibres, and we often observe exceedingly fine pale fibres running with dark-bordered fibres, the essential difference between these two classes of fibres in the same trunk being that the former fibre is nearer to its ultimate distribution than the latter; but in some instances it is probable that the fine fibre is a branch of the sympathetic. The fine fibre runs in the same transparent matrix (sheath) with the dark-bordered fibre. In fact the idea of tubular membrane or sheath being an essential and separate anatomical constituent of every individual dark-bordered fibre must be given up. For, as I showed in 1860, several dark-bordered fibres and fine fibres might run together in the same sheath or matrix. The opinion that the fine fibres which I hold to be nerve-fibres running in the same sheath with the dark-bordered fibres, are not nerve-fibres at all, but modified connective tissue, is, however, still entertained by many observers. As I have before stated, their continuity with true dark-bordered fibres may often be seen, and the same fibre may in some instances be followed to its ultimate distribution.

The different and incompatible views existing between continental observers and myself are in some measure due to this sheath question. The so-called sheath is not a "tube" or "membrane," or "tubular membrane," which contains the other constituents of the nerve-fibre; nor is it a sheath which invests them, but it is simply a transparent matrix, in which nerve-fibres, coarse and fine, are imbedded. The so-called sheath is not formed as a special structure to invest the nerve-fibres, but it results from changes occurring in the nerve-fibres themselves. This "sheath" or "tubular membrane" of the so-called dark-bordered fibre precisely corresponds to the transparent connective tissue, in which the fine nerve-fibres are imbedded. It is a form of connective tissue, and in many situations where nerves existed at an earlier period, nothing but this so-called sheath remains. All the soluble fatty matters have disappeared, and this material, which is not readily absorbed, is left behind. Vessels may waste, and ducts and glands may waste, and leave behind them the same sort of transparent connective tissue. Moreover, as I have before stated, it is altogether a fallacy to suppose that near the peripheral distribution, every single branch of nerve-fibre is surrounded by its own separate sheath. The drawings of the so-called axis-cylinder near the terminal distribution of the nerves also seem to me to be diagrammatic, founded rather upon a theoretical idea of the constitution of the nerve-fibre than upon the results of actual observation.

Many of the pale fibres accompanying the dark-bordered fibres are doubtless sympathetic fibres, for it has been shown that there are fine fibres springing from ganglion-cells which retain the same character from their origin to their distribution (see p. 236). Not only has the nervous nature of the fine fibres above described been proved by tracing them from their connexion with ganglion-cells, but a dark-bordered fibre has often been observed to be drawn out so as to form a line as fine as these fine

fibres. Indeed the observer often fails to trace an individual dark-bordered fibre for any great distance in consequence of its becoming exceedingly fine at the point where it crosses, or is crossed by other dark-bordered fibres. Not only so, but where a bundle of comparatively wide dark-bordered fibres passes through a small aperture, as for example in a bone, the fibres appear, as it were, drawn out to exceedingly thin threads, as represented in this figure.

And it may be fairly argued that since a wide dark-bordered fibre may be reduced in certain parts of its course to a fine cord not more than the $\frac{1}{50000}$th of an inch in diameter, without its integrity or conducting-power being interfered with, there is nothing unreasonable in concluding that fine fibres of the same diameter are efficient conductors of the nerve-current, although their length may be considerable. And I have shown that in many of the tissues of the frog (bladder, connective tissue, auricle, &c.), the finest branches of the nerves at their distribution are invariably less than the $\frac{1}{60000}$th of an inch in diameter. Is it then probable that the nerves distributed to the elementary fibres of the voluntary muscles of the limbs should form the single exception to this very general arrangement, and that the peripheral nerves of muscle should exhibit the dark-bordered character up to, or to within, a very short distance of their ultimate distribution or termination, as is maintained by many German anatomists.

Of the distribution of the pale nucleated nerve-fibres to the elementary muscular fibres.

Few anatomical questions have received of late years a larger share of attention than the ultimate arrangement of nerve-fibres in voluntary muscle. It is a matter of regret to me that although I have studied the question in many ways during the last five years, my conclusions do not accord with those of any other observer. And I must admit that although the German writers differ from one another on not unimportant points, they, nevertheless, agree in this, that the nerves form ends, pass into end-organs, or exhibit terminal extremities of some kind; while on the other hand my observations have led me to conclude not only that nerves never terminate in ends in votary muscle, but that there are no terminal extremities or ends in any nervous organ whatever.

With regard to the ultimate arrangement of nerves in muscle, the conclusions of Kölliker accord more nearly with my own than those of any other observer. (Compare Kölliker's statements in his Croonian Lecture delivered in 1862, with the results stated in my paper, published in the Phil. Trans. for 1860.) Kölliker agrees with me in the opinion that the nerves lie upon the external surface of the sarcolemma; but what he regards as ends or natural terminations, I believe to be mere breaks or interruptions in fibres which in their natural state were prolonged continuously.

And there is this further broad difference between foreign observers and myself, that while they consider that each elementary muscular fibre is very

sparingly supplied with nerves—a very long fibre receiving nervous supply at one single point only—I have been led to conclude that every muscular fibre is crossed by very delicate nerve-fibres, frequently, and at short intervals, the intervals varying much in different cases, but, I believe, never being of greater extent than the intervals between the capillary vessels.

My friend Kühne, of Berlin, has probably published more papers upon this vexed question than any other observer. He maintains that the nerve always passes through the sarcolemma and comes into direct contact with the contractile tissue*, or ends in protoplasmic matter which is in continuity with the muscle. He has, however, from time to time been led to modify his view very materially, as these figures, copied from his various memoirs published between the years 1862 and 1864, will testify. In his memoir published in 1862, he described minutely the structure of some very peculiar organs, which he stated had been demonstrated by him in connexion with the pale terminal intramuscular branches of the nerve-fibres. In more recent memoirs he seems to have abandoned the idea of the existence of those very peculiar bodies which he termed "Nerven-Endknospen," and with reason, since no other observer professes to have seen objects at all resembling those figured by Kühne. I should, however, state that the observations of Kühne have in the main been supported by Engelmann and some other observers.

In this Lecture I am unable to give even a brief account of the different views now entertained by the numerous observers who have studied this question; but in these drawings some of the most important are represented. A record of the opinions entertained by various writers will be found in Kühne's memoir, published in Virchow's 'Archiv,' vol. xxx. 1864; and I append the titles of some of the most important communications which have appeared since the publication of my first memoir:—

Kühne. Note sur un nouvel organe du système nerveux.—Comptes Rendus, Feb. 1861.

Kühne. Ueber die peripherischen Endorgane der motorischen Nerven. —Leipzig, 1862.

Theodor Margó. Ueber die Endigung der Nerven in der quergestreiften Muskelsubstanz.—Pest, 1862.

Kölliker. Untersuchungen über die letzten Endigungen der Nerven.—1862.

Rouget. Note sur la terminaison des nerfs moteurs dans les muscles chez les reptiles, les oiseaux et les mammifères.—Comptes Rendus, Sept. 20th, 1862; also Brown Séquard's Journal, 1862.

Naunyn. Ueber die angeblichen peripherischen Endorgane der motorischen Nervenfasern.—In Reichert und Du Bois Reymond's Archiv, 1862, p. 481.

* This view was first advanced by Kühne in 1859 ("Untersuchungen über Bewegungen und Veränderungen der contractilen Substanzen," Reichert und Du Bois Reymond's Archiv, 1860).

L. Beale. Further observations on the Distribution of Nerves to the Elementary Fibres of Striped Muscle.—Phil. Trans., June 1862.

Krause. Ueber die Endigung der Muskelnerven.—Henle und Pfeufer's Zeitschrift, 1863, p. 136.

Th. W. Engelmann. Ueber die Endigungen der motorischen Nerven in den quergestreiften Muskeln der Wirbelthiere.—Centralblatt f. d. Medic. Wissensch. 1863.

L. Beale. On the Anatomy of Nerve-fibres and Cells, and on the ultimate Distribution of Nerve-fibres.—Quarterly Journ. of Mic. Science, April 1863.

L. Beale. Further observations in favour of the view that Nerve-fibres never end in Voluntary Muscles.—Proceedings of the Royal Society, June 5, 1863.

L. Beale. Remarks on the recent observations of Kühne and Kölliker upon the termination of the Nerves in Voluntary Muscle.—Archives of Medicine, vol. iii. p. 25.

Th. Wilhelm Engelmann. Untersuchungen über den Zusammenhang von Nerv- und Muskelfaser.—Leipzig, 1863.

Kühne. Ueber die Endigung der Nerven in den Muskeln.—Virchow's Archiv, Band 27.

Kühne. Die Muskelspindeln.—Virchow's Archiv, Band 28.

Kühne. Der Zusammenhang von Nerv- und Muskelfaser.—Virchow's Archiv, Band 29.

L. Beale. An Anatomical Controversy. The distribution of Nerves to Voluntary Muscle. Do nerves terminate in free ends, or do they invariably form circuits and never end?—Archives of Medicine, vol. iv. 1865. Published separately: Churchill, London; Denicke, Leipzic.

L. Beale. On the Structure and Formation of the Sarcolemma of Striped Muscle, and of the exact relation of the nerves, vessels, and air-tubes (in the case of insects) to the contractile tissue of Muscle.—Trans. Mic. Society, 1864.

Rouget. Sur la terminaison des nerfs moteurs chez les Crustacés et les Insectes.—Comptes Rendus, Nov. 21, 1864.

As the observations of Kölliker, Kühne, and other observers in Germany, who followed me, were made upon the breast-muscle of the frog, while my first inquiries were instituted upon the muscles of the white mouse, I subjected this particular muscle of the frog to the same process of investigation which I had previously adopted in my researches in 1858–59, which were published in 1860. The results of these investigations will be understood by reference to these drawings, most of which were printed in my paper published in the Philosophical Transactions for 1862; and as explanations are appended to these figures, it is unnecessary to describe them more minutely here.

Although the results of this further inquiry (published in 1862) were favourable to the view I had advanced, they were deficient in this most

important point, viz. that the supposed network (as seen in this scheme) had not been conclusively demonstrated over the frog's muscular fibres generally. Near the point where the dark-bordered fibre divided to form pale fibres, a network was demonstated as is here shown, but it could not in many instances be traced for any great distance from this point. The following points, however, seem to me to have been established in this memoir:—

1. That the nerve-fibres, as I had already stated and as was confirmed by Kölliker, were outside the sarcolemma.

2. That the fibres might be followed for a greater distance from the dark-bordered fibre than they had been traced before, if the specimens were prepared according to the new method of investigation which I described.

3. The fine pale fibres were proved to be composed of several finer fibres, which resulted from the division of the dark-bordered fibre, and the pale fibres in the sheath of the nerve, which were also demonstrated for the first time.

4. Contrary to the statements of Continental observers, it was proved that the elementary muscular fibres of the frog were crossed at *numerous* points by nerve-fibres, and that the nervous supply to each elementary muscular fibre was much more free and uniform than was supposed. This fact may be demonstrated more especially in the thin muscles of the eye and in the mylohyoid of the frog.

Not satisfied with these results, I examined numerous other muscles of the frog and other animals, in the hope of being able to demonstrate the finest nerve-fibres in every part of their course over the sarcolemma, but was not able to obtain any muscle in the common frog sufficiently thin to trace the finest branches over a very considerable extent of surface. In the *mylohyoid* of the Hyla, however, I found a muscle eminently adapted for this investigation; and on June 5th, 1863, I presented a paper (published in the 'Proceedings') to the Royal Society upon the arrangement of the nerves in this beautiful muscle. I have prepared many specimens in which the nerve can be followed from one undoubted nerve-trunk to another, dividing and subdividing in its course, so as to form with other nerves a lax network of compound nucleated fibres, which compound fibres are often less than the $\frac{1}{60,000}$ of an inch in diameter.

The arrangement will be understood by reference to this drawing, which explains itself. I believe that no other explanation of the appearances observed in these specimens, than the one I have adopted, can be offered. In some of the muscles at the root of the tongue, the same arrangement has been demonstrated most distinctly.

More recently I have again studied the elementary muscular fibres from the breast-muscle of the frog, and have succeeded, in many cases, in tracing the fine granular nucleated fibres for a considerable distance. Near the margin of the muscle, I have recently succeeded in following a very fine fibre, resulting from the subdivision of a dark-bordered fibre, into fibres prolonged from what appear to be connective-tissue-corpuscles. The nuclei

of the network of fine nerve-fibres have often been mistaken for the connective-tissue-corpuscles beneath and, in some cases, amongst which they lie; and as old nerve-fibres, as well as other structures, degenerate and leave behind them what is called "connective tissue," a mistake is easily made unless the preparation be very clear*. In this drawing some very fine nerve-fibres, distributed to a portion of muscle at some distance from a dark-bordered fibre, are represented.

The distribution of nerves to the muscles of Articulata.

The highly elaborate and rapid movements of insects would lead to the inference that in them the distribution of nerves to the muscles must be very free. The textures are, however, so very elaborate, and their structure so minute, that the difficulty of demonstration must needs be greatly increased. Kühne's memoir, published in the year 1860, related to the distribution of nerves to the muscles of *Hydrophilus piceus*. He represented the nerve as perforating the sarcolemma, and being distributed almost in a brush-like manner to the contractile tissue. Subsequently he thought the nerve was connected with the line of muscular nuclei; but it was obvious that these were muscular, not nervous nuclei at all, and this view was abandoned. Some other observers have fallen into the same error. Although I have examined the muscles of many insects, and especially those of the *Hydrophilus*, I have been unable to confirm the observations made by some Continental observers.

For illustrating the distribution of nerves to the muscles of insects, I will select the common maggot, the larva of the blowfly. This insect can be obtained in all countries at almost all seasons of the year.

By reference to these drawings it will be seen that my conclusions accord in the most important particulars with those arrived at in my earlier investigations. The drawing-out of the sarcolemma into a sort of eminence at the point where the nerve commences to ramify over it, is well seen in these two figures. This has been mistaken for a special organ by Kühne (Nervenhügel); and it has been inferred that the nerve perforated the sarcolemma at this point.

In his paper in the 'Comptes Rendus' for November 21, 1864, M. Rouget in part confirms my statements regarding the structure of Kühne's 'Doyère'schen Nevenhügel,' and states that, at the Nervenhügel, the nerve-fibre divides into two fine fibres, which may be traced for some distance, and then terminate. "Leur extrémité terminale est légèrement effilée; elle ne présente ni plaques, ni noyaux, ni substance finement granuleuse."

The structure of these so-called Nervenhügel in insect-muscles was described and figured by me in a paper, accompanied by several drawings, read to the Microscopical Society on June 1, 1864, and published in the 'Transactions' on October 1, 1864. Although M. Rouget agrees with me

* This part of the question is considered in my paper published in the Philosophical Transactions for 1864, page 565.

as respects the nature of the Nervenhügel, we are at variance upon the further course and mode of termination of the nerve-fibre, M. Rouget maintaining that it penetrates beneath the sarcolemma and there terminates in a very fine fibre, in contact with a very limited portion of the contractile tissue, while I have been able to trace the nerve for a long distance beyond the point at which he makes it end, and I have seen it dividing into very fine fibres, which form an extended network upon the sarcolemma, as represented in this drawing, to which I beg to direct special attention. M. Rouget's researches lead him to conclude that the arrangement of the nerves in the muscles of Articulata is totally distinct from that met with in Vertebrata. "Il résult de ces faits qu'il n'y a pas d'identité entre les divers modes de terminaison des fibres nerveuses motrices chez les vertébrés et les articulés." On the other hand, my observations lead me to the conclusion that the arrangement is in its essential points the same in all classes of animals. In no case are there nerve-ends, but always plexuses or networks, which are never in structural continuity with the contractile tissue of the muscle.

I have particularly studied the arrangement and distribution of the nerves in the leech. The same facts noticed in p. 258 on the *branching* of nerve-fibres, are observed in the nerves of this animal; and I have been able to obtain many specimens of nerves which could hardly be distinguished from some of the finest dark-bordered fibres of the higher animals. Some of the muscular fibres of this animal are very thin, and are separated from one another by considerable intervals, in which the ramification of exceedingly delicate nerve-fibres can be readily detected, and the nerve-fibres can be followed to their connexion with ganglion-cells. I have made many specimens of the muscles of the leech, and taken several drawings to illustrate these points, but I regret that I am unable to have these copied for this memoir.

Of the structure of the bodies termed nerve-tufts, nerve-eminences, and Nervenhügel, seen in connexion with certain muscular nerves.

I propose now to consider the structure of the peculiar bodies in connexion with the nerves distributed to the muscles of certain animals, described by Kühne, Rouget, Krause, and others. These differ from the bodies first studied by Kölliker in the breast-muscle of the frog, which are referred to in p. 261. I have never been able to demonstrate such bodies as I am about to describe in the muscles of animals generally, although they are exceedingly distinct in the muscles of lizards, as shown by Rouget. I have demonstrated many in the cutaneous muscles of the neck, and in the muscles of the tongue of the chameleon, and shall carefully consider the structure of these.

In the first place, I would remark that these bodies are *external to* the sarcolemma, as may be proved by examination of the specimens. The course of the nerves *to* and *from* these bodies almost renders it impossible

that they could be beneath the sarcolemma, while in many cases the outline of the sarcolemma can be followed underneath them. Secondly, it appears probable that they are a reduplication and expansion of continuous fibres, rather than terminal organs formed upon the extremities of the nerve-fibres; nor would it seem that these organs are essential to the action of nerves upon muscle, since they are only to be demonstrated in the muscles of certain animals. Moreover, as many different forms of these nerve-organs are to be seen in a small piece of muscle, exhibiting different degrees of complexity, we may perhaps by studying them attentively be able to draw a true inference as to their real structure and the mode of their formation.

Kühne's idea of the structure of these bodies is represented in this diagram, which has been copied from his last paper. The interpretation of the appearances here given is totally different from that which I have been led to offer. In my specimens the nerve-fibres entering into the formation of these tufts are seen to divide and subdivide into several branches, which are folded, as it were, upon one another. The fibre in many instances does not consist of the axis-cylinder only, but the white substance may also be detected in connexion with some of the fibres. The nuclei seem to be connected with the finer branches of the nerve-fibres. In fact the organ seems to consist partly of broad fibres, partly of fine fibres formed by the branching, spreading out, and coiling of the fibres resulting from the subdivision of the original nerve-fibres which enter into the formation of the tuft. Moreover I have succeeded in demonstrating that, from various points of the oval coil, branches pass off and run on the surface of the sarcolemma, probably passing on to other nerve-bundles. These fine fibres, which are represented in my drawings, have not been delineated, as far as I am aware, by any previous observer who has examined these bodies. In connexion with every nerve-tuft there seem to be *entering* and *emerging* fibres; and in the majority of instances, fine fibres may be traced from the tuft in several different directions.

When the nerve-tuft is formed, as it were, upon the trunk of the fibre, the entering fibres are more numerous and larger than the emerging fibres. This is probably to be explained by the circumstance that some fibres pass away from each tuft upon the surface of the muscle, and thus establish communications with nerve-fibres which approach the elementary muscular fibre at other points. This drawing explains how, as the muscular fibre grows, the bundles marked *a* and *b* become separated further and further from one another, and the fine communicating fibres connecting them necessarily become so very much drawn out that they are too delicate to be seen upon the surface of the sarcolemma.

And now it must be obvious that these bodies precisely correspond to the bendings and division of the fine dark-bordered fibres at the point where they come into contact with the surface of the sarcolemma, in the breast- and other muscles of the frog. At this point there is always a twisting of fibres with free branching, and the formation of a number of exceedingly

delicate nerve-fibres, the nuclei or masses of germinal matter being very close together, so that a considerable number are to be observed within a comparatively small space. Here a complex network of fibres, the meshes of which are very small, is found. But this plexus or network is not terminal, nor does it result from the branching of a single fibre, as has been represented. *Many fibres* enter into its formation ; and from various parts of it long fine fibres pass off to be distributed upon the surface of the sarcolemma. This is explained in these figures from the frog, from the white mouse, and in this one from the maggot.

It seems most probable that at the situation of these coils the contraction of the muscular fibre would commence, and that, from the nerve-current traversing several fibres collected over a comparatively small portion of muscle, the contraction at these points would be most intense, while it is probable that the contractions commencing at these points would extend, as it were, from them along the fibre in opposite directions.

I consider these nerve-tufts therefore simply as collections of nerve-fibres, differing only from the ordinary arrangement before described, somewhat in the same manner as the compressed nerve-network in a highly sensitive papilla differs from the lax expanded nerve-network in the almost insensitive connective tissue.

Of the arrangement of the nerve-fibres in other forms of striped muscle, as the branching fibres of the tongue, the muscular fibres of the heart, and lymphatic hearts of the frog.

To certain forms of striped muscle in which no distinct membranous tube of sarcolemma can be demonstrated, nerves are freely distributed ; but all attempts to demonstrate end-organs or terminal extremities in such textures have hitherto failed. In the heart the existence of delicate nerve-fibres arranged to form networks is distinct ; and perhaps the most favourable locality for demonstrating these fibres is the auricle of the frog's heart. Bundles of exceedingly fine nerve-fibres, much resembling those in the bladder, can be seen running in different directions and branching amongst the delicate networks of exceedingly fine muscular fibres. Very fine fibres may be observed in thin specimens with the aid of high powers, crossing the fine muscular fibres at different angles, then dipping down in the intervals between them, and being soon lost in consequence of their ramification in the deeper layers.

In this drawing the relation of the nerve-fibre to the finest part of some of the branching muscles of the tongue is represented ; and I have observed an arrangement precisely similar in the case of the muscular walls of the lymphatic hearts of the same animal. The very thin and narrow muscular fibres of the heart and tongue would appear to offer very many advantages for the demonstration of ends and end-organs, supposing them to exist ; but the most careful observation under the most favourable circumstances and with the aid of the highest powers, reveals only delicate nu-

cleated nerve-fibres, forming lax networks, branches of which may often be followed for a very long distance, and then traced into neighbouring nerve-trunks.

Of the finest nerve-fibres which influence the muscle.

It is probable that the active part of the nerve-fibre, as regards the elementary muscular fibre, commences only at the point where the dark-bordered character of the nerve-fibre ceases, and therefore that the most important and most active portion of the peripheral nerve-fibres distributed to muscle, has escaped the observation of many observers. The fibres are extremely delicate, and, like other very fine nerve-fibres, can only be rendered visible by special methods of preparation. Probably every fibre, however fine, is compound, being composed of several finer fibres. Nuclei are invariably found in relation with these fibres, and they vary in number in different cases. The structure and general appearance of the finest nerve-fibres will be understood by reference to the figures.

From the foregoing observations I conclude that the nerve-fibres which are to be regarded as the fibres of distribution are far more delicate and much finer than has been hitherto supposed. The remarks which I make on this head with reference to the ultimate nerve-fibres distributed to voluntary muscle, will apply to the ultimate nerve-fibres distributed to other organs.

In mammalia the ultimate fibres appear as narrow, long, slightly granular, and scarcely visible bands with oval masses of germinal matter, situated at short but varying intervals, as described in my paper published in the Phil. Trans. for 1860. In many reptiles (frog, newt, lizard, snake, chameleon), however, these ultimate nerve-fibres are narrower but much firmer than in mammalia; and they are more readily demonstrated, as they do not give way under the influence of considerable pressure and stretching. Although fine nerve-fibres have been described in certain situations before I drew attention to these fine pale nucleated fibres in muscle, it was not generally supposed that the active peripheral portion of nerves exhibited these characters; nor indeed has this fact yet received the assent of many distinguished anatomists. The arrangement of the fine nerve-fibres in the summit of the papillæ of the frog's tongue, described in my last paper presented to the Royal Society (Phil. Trans. June 1864), and in the mucous membrane of the human epiglottis, will, I venture to think, tend to convince many that the really active peripheral portion of the nervous system consists of excessively fine nucleated nerve-fibres arranged as a plexiform network.

With reference to the diameter of these finest branches of the nerve-fibres, many can be demonstrated and followed for long distances which are less than the $\frac{1}{100000}$th of an inch in diameter; and there is reason to think that fibres much finer than this actually exist, and serve as efficient conductors of impressions to and from nerve-centres and peripheral parts.

The Essential Structure of a Nervous Mechanism considered.

Of the supposed terminations of the dark-bordered nerve-fibres, and of the probable existence of nerve-circuits.

It will have been remarked that Continental observers are unanimous in representing the dark-bordered nerve-fibre as passing to its destination unaccompanied by any other fibre whatever. In some drawings it is represented as terminating in a short fine fibre, which is regarded as the prolongation of the axis-cylinder; in others, this fine fibre is represented as bifurcating so as to form two very fine fibres. Some observers consider that the "axis-cylinder" spreads out to form a band which is more or less convoluted, but terminal, forming an "end-organ," while others hold that the fibre gradually ceases or loses itself in the surrounding tissue.

But while there are these minor differences, all agree in the opinion that the nerve-fibre passes alone to its ultimate "end." On the other hand, I have endeavoured to show that at least one fine nerve-fibre accompanies the dark-bordered fibre to its ultimate destination (page 241) as represented in these figures, and that this fine nerve-fibre is a constant structure of great importance. It was first fully described by me in papers in the 'Archives of Medicine' on the frog's bladder; but its existence was referred to in my paper in the Philosophical Transactions for 1860, and its arrangement investigated in that published in the Philosophical Transactions for 1862.

Some surprise may be felt that Continental observers have not specially noticed the fine fibre accompanying the dark-bordered fibre, or referred to my statements concerning it; but as neither the fine fibre, nor indeed the finest part of the dark-bordered fibre, can be seen in specimens examined in aqueous fluids, it was scarcely to be expected that the facts I have described should have been verified in Germany. I therefore beg to direct the attention of anatomists and physiologists to the drawings to which I now point, and to my specimens.

The fine fibre accompanies the dark-bordered fibres distributed to the tissues of the frog generally, but it is more easily demonstrated in relation with the nerves distributed to the bladder, to the mucous membrane of the palate, the skin, and the connective tissue about the heart and lungs, than with those of striped muscle; it is, however, so frequently seen in the case of muscular nerves, especially in the mylohyoid of the Hyla, that I believe it is invariably present, though it cannot be *demonstrated* in all cases. Not only is the structure of the fibre very delicate, but it is often obscured by the dark-bordered fibre which it accompanies.

Now, if a single fibre passed at once to its destination, as Continental observers suppose, it is obvious that the arrangement of the nerves in muscle must be different in principle to their arrangement in the cornea, for example, where it is admitted no "end-fibres" can be detected. But, on the other hand, as at least two fibres, and usually several, pass together to

their ultimate destination, there is at least a possibility, if not a reasonable probability, that the ultimate arrangement of nerve-fibres in muscle, the cornea, and other tissues is, in principle at least, the same. It may be remarked, further, that it is not likely that the nerve-current would be running in the same direction in two distinct fibres situated close together, while the existing anatomical arrangement above referred to is suggestive of currents passing in opposite directions. This view is favoured by the fact of one fibre being much finer than the other—an arrangement which would be fully explained if each of the two fibres were a part of two different circuits. My meaning will be understood at once if this diagram, to which I now point, be examined.

I have endeavoured to prove that in various forms of muscular tissue, and in other textures, nothing but *continuous* nerve-fibres can be observed. The most careful observation has failed to show any appearance which could be considered as demonstrative of "*ends*" of any kind; and although in many cases I have been unable to follow the very fine fibres resulting from the division of the nerve-fibres of one trunk into those of another trunk—although, therefore, there is, as it were, a hiatus in the evidence advanced in favour of this view being universally applicable, the appearances in every one of the cases that I have examined are such as to render it almost certain that this is the real arrangement. If we find a compound nerve-trunk passing to one part of a muscle and another compound trunk passing away from another part of the muscle, in such manner as would be easily explained upon the supposition that certain of the fibres of one cord were continuous with those of the other—more especially if the action of these fibres could be explained upon such an hypothesis, we should surely be justified in inferring the continuity of the fibres, although we could not trace them through their entire course. It might be urged by an objector, that it is just at this intermediate point in many instances that the evidence fails. But it must be borne in mind that it fails in certain instances only; for I have traced and can demonstrate, in some of my specimens, the nerve-fibres distributed to muscular tissue in every part of their course. The truth of my statements upon this anatomical question is in fact admitted in the case of certain muscles; and those who still maintain that nerve-fibres "*end*" in voluntary muscle must maintain that there are some muscles in which nerves form networks, while in others they terminate in distinct ends—that in fact nerve-fibres are distributed to different kinds of muscular tissue upon at least two very distinct principles, although no differences whatever can be shown in the essential structure or action either of the muscular or of the nervous tissue.

But the case is still stronger than this. I shall adduce a considerable amount of collateral evidence in favour of the view that nerves form continuous and uninterrupted cords; and this evidence will be derived from many different sources.

As there is the greatest difference of opinion with regard to the arrange-

ment of the nerves in muscle, and as the question is now much involved, it seems to me of the utmost importance to consider it from a general point of view. Every careful examination that I have made with the view of ascertaining the arrangement of the nerve-fibres in various tissues has tended to confirm me in the opinion that networks and continuous circuits exist, and that there are no " ends " or " terminal extremities." Although I am of course ready to admit that no amount of argument from general considerations can upset the conclusions resulting from direct observation in special cases, I submit that the conclusions of my opponents, in the particular instances advanced by them, have never been supported by positive demonstration. Indications of the appearances they have described undoubtedly exist; but it seems very difficult to prepare specimens which shall admit of but one interpretation, and so distinct that several independent observers would, upon examination, arrive at one and the same conclusion. It is too often urged that the specimens demonstrating " ends " and " end-organs " do not "keep," and must be examined when quite fresh, while I find no difficulty in preserving those which demonstrate " networks " and "plexuses." I desire, however, to weigh carefully every kind of evidence that can be brought to bear upon the determination of this point, which is undoubtedly one of very great difficulty. As the question, too, is a fundamental one of the utmost importance, it is worthy of the most patient consideration.

Of terminal plexuses and networks of fine nerve-fibres in the cornea and in connective tissue.

From its transparency, the simplicity of its structure, and the absence of vessels over at least a great part of its extent, the cornea of the smaller lower animals presents many advantages for studying the arrangement of the ultimate nerve-fibres. My friend and former pupil, Prof. Ciaccio, now of Naples, very carefully studied this subject; and the results of his observations will be found in the Transactions of the Microscopical Society for July 1863, " On the Nerves of the Cornea, and of their distribution in the Corneal Tissue of Man and Animals," by Prof. G. V. Ciaccio, M.D., of Naples. Of the existence of nerve-networks in this tissue there can be no question; but there is some difference of opinion regarding the manner in which the ultimate nerve-fibres are arranged. This drawing represents the nerve-fibres in the cornea of the Hyla. The relation of the finest nerve-fibres to the corneal corpuscles is a question of great importance. Kühne has endeavoured to prove that the ultimate nerve-fibres are continuous with the processes of the connective-tissue-corpuscles, and that there is an actual continuity of tissue, such as he believes exists between the nerve-fibre which perforates the sarcolemma of muscle and the protoplasmic matter which is in actual contact with the contractile tissue.

Careful observation, with the aid of the $\frac{1}{25}$ and $\frac{1}{50}$-object-glasses, has convinced me that there is no such arrangement as Kühne supposes, but

that the nerve-fibres pass over or under the prolongations from the corneal corpuscles without being continuous with them. The fundamental arrangement here seems to be the same as elsewhere. The nerve-fibres run amongst the tissue, but they are continuous neither with the proper fibrous tissue of the cornea, nor with its nuclei; and if any influence is exerted by the nerve upon the tissue or upon the nuclei, it is probably effected by the current which is transmitted by the fibre, and is not due to any direct continuity of texture.

The figure to which I now point, represents a thin layer of the connective tissue covering the posterior part of the mylohyoid muscle of the Hyla, with the nerves and vessels. The bundles of fine dark-bordered fibres can be very readily distinguished from the fine fibres given off from them and forming a very extensive network in every part of the tissue. In this specimen, fibres can be traced from the nerve-trunks to the capillaries, as well as to the nerve-network of fine fibres imbedded in the connective tissue. If the reader imagines muscular fibres placed in the meshes of this network, he will, I believe, have a correct idea of the manner in which nerve is distributed to muscle. (See figure on opposite page.) The same facts are demonstrated in my specimens of connective tissue from the abdominal cavity of the frog, the outer surface of the lungs, &c.

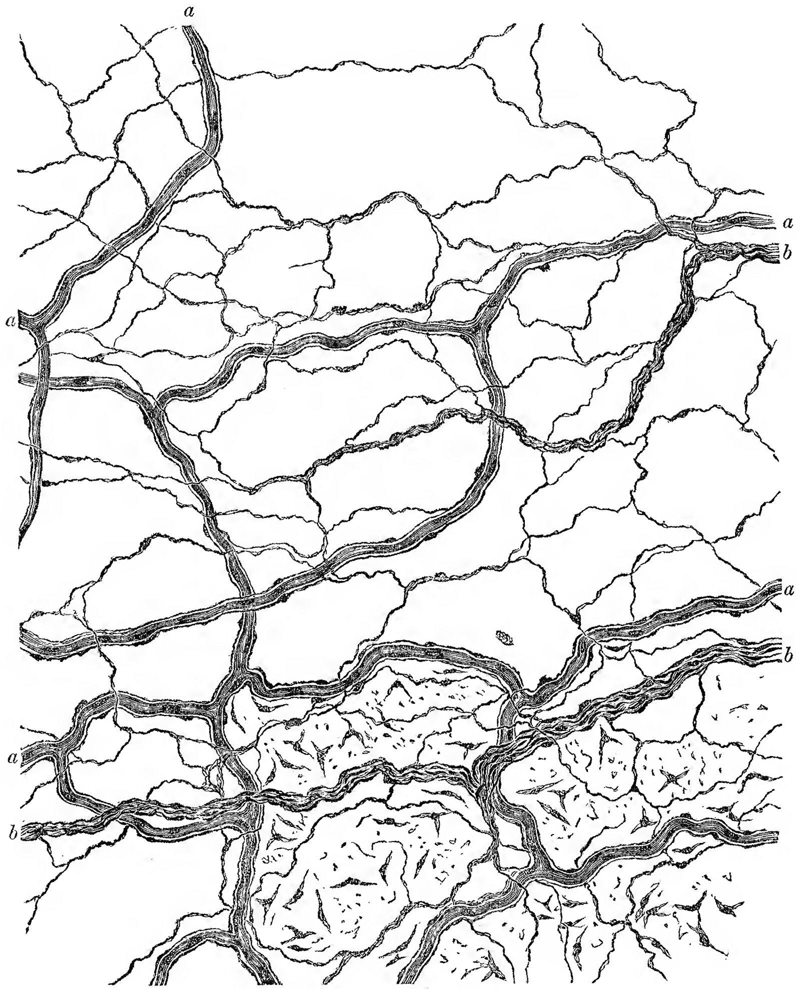
The distribution of the finest nerve-fibres to the mucous membrane of the epiglottis of the human subject is also upon the same plan, but the finest nerves are more difficult to demonstrate. In this figure the capillary vessels and the nerves, as they lie immediately beneath the epithelium, are represented; and in this one a small portion of the tissue cut exceedingly thin, from one of the intervals between the capillaries, is represented magnified by the $\frac{1}{25}$.

Fine nerve-fibres distributed to capillaries in the form of networks and plexuses.

It has been already shown that fine nerve-fibres are distributed to the cornea, to the fibrous tissue in the abdomen of the frog, and to that of the pericardium and of other parts, which is destitute, or nearly destitute, of vessels, and which at the same time is a tissue which can scarcely be regarded as being more immediately influenced by nerve-fibres than the ordinary forms of cartilage, which are undoubtedly destitute of them. To assert that these fibres are in some manner directly concerned with the *nutritive process* is begging the question; and as cartilage is undoubtedly developed and nourished without the direct influence of nerve-fibres, it is probable that the nutrition and development of such tissues as the above, which are closely allied to cartilage, do not depend upon the nerve-fibres which are distributed to them. These nerve-fibres probably perform a totally different service.

Pale nucleated nerve-fibres are also distributed to capillary vessels, as is well shown in the figures to which I now direct attention. That the fibres

seen in the specimens from which these drawings have been taken are true nerve-fibres, is proved by the circumstance of their having been followed from or into undoubted nerve-trunks. The evidence I have adduced in



Connective tissue covering part of the mylohyoid muscle of the frog, and extending from its posterior portion. *a*. Capillary vessels, with their nerve-fibres. *b*. Bundles of fine dark-bordered nerve-fibres, from which fine nerve-fibres may be traced to the capillaries, and to their distribution in the connective tissue, where they form networks of exceedingly fine compound fibres. The engraving represents the specimen as magnified only 110 diameters; but the original drawing was taken from it when magnified by a much higher power.

favour of this view, is of the same nature as that which is admitted to prove

the nervous nature of the fibres distributed to muscle itself; indeed, if these fibres distributed to the capillaries are not nerve-fibres, none of the fine fibres in the cornea, fibrous tissue, &c. already alluded to and represented in my drawings, are nervous. Fine nerve-fibres can be followed from the nerve-trunk, and traced to their distribution on capillary vessels, as represented in this drawing, and as I have also shown to be the case in my Memoir "On the Papillæ of the Frog's Tongue," presented to the Royal Society in June 1864. Some of the fibres can be traced from the immediate neighbourhood of the capillary, where they for the most part ramify, in the surrounding tissue, and may be followed to the point where they pass into undoubted nerve-trunks.

With reference to the office performed by these nerve-fibres, a careful consideration of all the facts I can ascertain in connexion with this question, leads me to the conclusion that these fibres, close to the capillary vessels and in tissues destitute of capillaries, are not concerned in special sensation, but are the afferent fibres to the nerve-centres in which the efferent fibres distributed to the small arteries take their rise. I believe that these fibres do exert an influence upon the process of nutrition, but only by their indirect influence upon the nerves which govern the calibre of the small arteries transmitting the nutrient fluid to the capillaries nearest to the tissues in which they ramify.

Although time precludes me from entering into this part of the inquiry, I may be permitted to allude briefly to the mechanism which I believe is concerned in regulating the nutritive process, as it occurs in the tissues of man and those higher animals whose nutritive operations continue to be carried on with comparatively little alteration under very varying external conditions. The arrangement I am about to describe appears to be, within a certain range of variation, *self-adjusting*. If, however, the limits be overstepped in either direction, as not unfrequently happens, under the very artificial conditions to which man and many of the domestic animals are exposed, the range of self-adjustment is exceeded, and oftentimes a part of the mechanism is completely destroyed and can never again be effectually repaired or replaced.

It is obvious that the afferent fibres above referred to, must be affected by any alterations occurring in the flow of pabulum to the tissue in their immediate neighbourhood. Suppose, for example, the quantity of nutrient pabulum flowing to the cells of a tissue to which nerve-fibres of this class are distributed, to be unusually great, these nerve-fibres would necessarily be compressed by the swelling of the surrounding elementary parts which absorb the pabulum. This pressure would, in the first instance, so affect the nervous centre as to cause a change in the condition of the efferent nerve-fibres, which would induce contraction of the small arteries transmitting the blood to the capillary vessels, and thus the quantity of pabulum sent to this locality would be immediately reduced. The nuclei of the nerve-fibres would also participate in the increased absorption of nutrient

matter; but precisely in what manner, I must not now discuss. If, however, the conditions which led in the first instance to the increased nutrition persisted, the pressure upon the nerve-fibres might go to the extent of paralyzing them, in which case the small arteries would become dilated; the capillaries must in consequence be fully distended with blood, and that congestion which constitutes one of the earliest stages of inflammation as it occurs in man and the higher animals, would result.

I have already indicated the wide differences in structure, mode of growth, and in the changes occurring during action, between the spherical and oval nerve-cells, and the so-called caudate nerve-cells. These differences are sufficiently marked to justify me in regarding them as two distinct classes of central nerve-cells performing very different offices or functions*.

Several considerations have led me to conclude that the oval and spherical ganglion-cells are the sources of nervous power, while the so-called caudate nerve-cells in the cerebro-spinal centre are the points at which several different nerve-circuits intersect, and probably act and react upon one another. The marvellously complex and combined nervous actions depend, in all probability, upon the perfection attained by this latter part of the nervous mechanism. I have been led further to the opinion, not only that the spherical and caudate nerve-cells are concerned with the reflex phenomena of the vascular system, but that those forming the ganglia on the posterior roots of the spinal nerves are intimately connected with the general reflex actions occurring in the voluntary muscles when the cord is divided transversely. From the arrangement of the vascular nerves distributed to the vessels of muscles, it is easy to understand how, by an increased action of these vascular nerves, the contraction of the muscles of a limb might be caused. I have demonstrated that connexions exist between the peripheral portion of purely sensitive nerves and the nerve-fibres distributed to the tissues in which capillaries ramify, as well as to capillary vessels themselves. These connexions would account for the excitation of involuntary reflex actions by the application of a stimulus to the general cutaneous surface. If this view be correct, the ganglia on the posterior roots of the nerves, rather than the different segments of the spinal cord, must be regarded as the centres of reflex actions and also as the nervous centres which, with the so-called sympathetic ganglia, preside over all the vascular, and, through the vessels, over the nutritive phenomena of the body. The facts and arguments in favour of these general conclusions will form the subject of a separate memoir.

Arguments in favour of uninterrupted circuits, deduced from an examination of the trunks of nerves, and arrangement of nerve-centres.

One is somewhat surprised that the mode of branching of nerves, referred to generally in pp. 239, 240, which is so universal, has not been dwelt upon

* See my paper "On the Apolar, Unipolar, and Bipolar Nerve-cells," &c., Phil. Trans. 1863, and a paper entitled "Indications of the Paths taken by the Nerve-currents," &c., Proceedings of the Royal Society, vol. xiii. p. 386.

and carefully described by those who have written upon the structure and arrangement of nerves. The nerves distributed to a tissue or organ are often represented as if they all passed straight to their terminal distribution, while the invariable arrangement is such as to lead to the inference that, of the fibres composing a bundle of nerves, some are proceeding in a direction *from*, and others *towards* the nerve-centre or peripheral part; and this is observed not only in purely motor, but in purely sensitive, as well as in mixed nerves. It is also found in the case of the sympathetic system, and is to be demonstrated in all animals. It is, however, not possible to dissect the trunk of a fine nerve and render it sufficiently transparent to display these facts, if the ordinary methods of examination be adopted; but by the plan of investigation I have fully described, the arrangement may be readily demonstrated in the nerves either of the higher or lower animals, although with the greatest facility in the Hyla*. Few anatomical facts seem to me of more interest and importance in their general bearing upon the physiology of the nervous system than that above alluded to. Its constancy proves its importance, if it does not alone compel us to infer that it is essential. What explanation, then, can be offered of the three sets of nerve-fibres which can invariably be traced at the point where a nerve-fibre comes off from a trunk passing at right angles to it, as represented in these figures? Look at it how we may, there must be three sets of fibres in all cases; and just as we find that the nerve-fibres constituting the roots of the nerves divide soon after their entrance in the spinal cord into bundles which pursue many different directions—some passing upwards towards the brain, others downwards towards the lower segments of the cord, and some to the opposite side, as has been well shown by the researches of Lockhart Clarke—so in the case of every nerve-fibre which appears to pass into or come from an adjacent nerve-trunk, fibres pursue three different courses, as shown in these drawings.

These may be *afferent*, *efferent*, and *commissural*; and there are fibres commissural as respects different parts of the peripheral system as well as of the central organ. Thus, I believe, may be explained the action of each papilla as a separate organ, independently of its neighbours, or the harmonized action of several different papillæ. By the same arrangement I consider the harmonious action of the several elementary fibres entering into the formation of muscle is effected.

As has been before observed, the large compound nerve-cords or trunks, the finer bundles, and the finest constituent fibres of the pale terminal nerve-fibres exhibit the same general arrangement. The remarks already made with reference to the course of the fibres in the nerve-trunks and the branching of the dark-bordered fibres, also apply to the finest fibres; and at the point where a fibre passes off from another at right angles, the existence of the three sets of fibres can be demonstrated. I would draw

* How to work with the Microscope. Third Edition, p. 204. See also "On the Branching of Nerve-trunks," &c., Archives, vol. iv. p. 127.

attention to the arrangement shown in these drawings, and especially to that represented in this figure; not that I would maintain that in the finest fibres these three fibres are separated from one another or insulated by a layer of white substance, but, on the contrary, I consider that in many cases these fine fibres, although they may often be split in the longitudinal direction, nevertheless in their natural state form almost homogeneous fibres, the material of which may permit the passage of nerve-currents in the different directions indicated. It is very probable that the passage of the currents along precisely the same paths for a considerable time may cause the decomposition of the nervous matter in such a manner as to give rise to distinct lines, which might readily be mistaken for separate fibres, and after a time lines of fibres in an apparently transparent tissue would result*. At an early period of development, nerves form a sort of thin expansion, in which the appearance of fibres crossing one another in various directions may be afterwards produced by the passage of the nerve-currents. Beneath the external investment of the common fly and many other insects, and beneath the soft, delicate perivisceral membrane of mollusca, I have seen the most beautiful and elaborate arrangement of apparent nerve-fibres of such a character as to justify the above inference.

In the cornea, that part of some of the nerve-fibres from which several fine bundles radiate in different directions exhibits lines or fibres crossing one another in every direction which the emerging fibres take.

This subject is capable of much further elucidation, and is well worthy of being considered in detail; but in this Lecture I only allude to it cursorily because it bears, in a most important manner, upon the question of uninterrupted nervous circuits, and affords an explanation of the manner in which the complex arrangement which nerves ultimately exhibits is brought about.

Of the "termination" of nerves in papillæ and in special cutaneous nervous organs, such as the papillæ concerned in touch and taste, and in the Pacinian corpuscles.

Now in highly elaborate nervous organs like the papillæ of the frog's tongue, which are very minute, and situated comparatively close to one another, we have an opportunity of studying, under great advantages, the course pursued by the constituent fibres of a bundle of nerves. And although even here it is not possible to follow a single fibre for any great distance, a careful consideration of what can be demonstrated leads to the inference that to every one of these papillæ three sets of nerve-fibres are distributed.

I have always been able to demonstrate in the peripheral organs that I have examined more than a single nerve-fibre; and where, as is almost

* Indications of the Paths taken by the Nerve-currents, &c.: Churchill and Sons.

invariably the case, numerous terminal organs exist, these are always connected together by nerve-fibres which pass from one to the other. Although the arrangement is not always so distinct as represented in this drawing of the papillæ from the tongue of the frog, I always find that where a nerve-trunk divides into two sets of branches, there exists at the point of division a fibre or fibres which seem to connect the two terminal organs to which the bundles of fibres pass. Passing to every touch-body in the papillæ of the skin of the finger, I find more than one nerve-fibre; and the corpuscle itself seems to consist of a very much coiled and reduplicated nucleated nerve-fibre, as represented in this drawing.

In the peripheral cutaneous nervous organs of many invertebrate animals which I have examined, especially in some of the insects and annelids, I find a *bundle* of nerve-fibres, not a *single nerve-fibre*, as is usually represented. This drawing illustrates the view generally entertained; and this one, my own inference of the structure of these organs. Even in the Pacinian body I find no such indications of a true *termination* of the axis-cylinder as is usually described: not only so, but in many cases I have seen three or four very wide lobe-like continuations of the axis-cylinder bending downwards from its highest point, and passing apparently into very fine granular fibres which lie between the laminated capsules, and are continued into the nerve-sheath. The drawing will illustrate the structure of all these allied peripheral nerve-organs, according to my observations.

Evidence in favour of continuous nerve-circuits, derived from the study of the development of nerve-fibres distributed to muscle.

The development of nerves distributed to muscle is most difficult to investigate, but it is a subject well worthy of most attentive study; and although I cannot hope to give a clear account of the process, I shall make an attempt to describe what I have myself seen. The relation of nerves to the contractile tissue of muscle and other tissues, and the general arrangement of nerve-fibres, having been determined, one cannot avoid asking how the fibres became arranged as we see them in the fully formed texture.

Of the part taken by the masses of germinal matter there cannot be the slightest doubt; for it can be shown most conclusively that as the nerves advance from the early to the complete stage of their development, the distance between the several masses of germinal matter gradually increases. This may be proved in the case of dark-bordered as well as of very fine nerve-fibres. It is well shown in these figures. At an early period of the development of muscle, very numerous masses of germinal matter are seen amongst the muscular fibres, in which transverse markings are already developed. These, as I have been able to satisfy myself by researches upon the diaphragm and intercostal muscles of the fœtal dog, are concerned in the formation of nerves and capillaries.

In the young caterpillar the surface of some muscular fibres seems to be

completely covered with nuclei; and as development advances these nuclei or masses of germinal matter seem to separate further and further from one another, and the delicate nerve-fibres might be said to be drawn out from them. At the same time the muscular fibre increases in size. It will probably be conceded that at an early period of development of a muscle there are masses of germinal matter taking part in the development of the three different structures—*muscle, nerves,* and *vessels.* Besides these, upon the surface of the muscle, and between the muscular fibres, are masses which have perhaps already given rise to the formation of a soft granular and slightly fibrous connective tissue. I think that these last masses have originated from the same parent masses as the others. Indeed it is certain that this must be so. Of the masses taking part in the development of a bundle of nerve-fibres, those on the surface produce not true nerves, but connective tissue, and so with regard to muscles, vessels, and other textures.

The part taken by the germinal matter in the development of muscles, nerves, and vessels may be studied in the fully-formed frog, and with greater facility than in the embryo. At certain intervals amongst the large muscular fibres of the frog may be discovered with some difficulty some bundles of finer muscular fibres. These are most distinctly seen, however, in the thin breast-muscle of the frog, where they were discovered by Kölliker. They were termed by him "*nerve-tufts,*" and are figured in his *Croonian Lecture,* delivered in 1862 (Proceedings of the Royal Society, 1862, p. 78). I have had Kölliker's figure copied. It does not, however, represent all that may be seen in these swellings, prepared according to the particular plan before alluded to (p. 258); for the numerous oval nuclei, figured in Kölliker's drawings, are represented by him as being pretty generally diffused throughout the swelling, and as not being connected with one another, or with any definite structure. The relation of the nerve-fibres to these nuclei is not indicated in Kölliker's drawing, nor is the meaning of these numerous nuclei discussed.

Some of the nuclei (masses of germinal matter), however, are seen in my specimens to be nuclei in the course of very fine nerve-fibres—nuclei which take part in the formation of the nerve-fibres themselves. Others are the nuclei of the muscular fibres which are undergoing development, and over the surface of which the fine nerve-fibres are spread out. These facts are demonstrated in several specimens which I have mounted in strong glycerine and acetic-acid syrup*. A portion of one of these is represented in the figure to which I now point. This drawing, which is magnified 700 diameters, appears somewhat confused, owing to the very close proximity of the nerves to the muscles. It is, however, a careful copy of one of my specimens just at the spot where *three* dark-bordered nerve-fibres pass into, or emerge from, one of the "nerve-tufts." In this drawing I have shown one branch of a dark-bordered nerve-fibre and its division into two very fine

* "I have found this strong acetic-acid syrup a most valuable agent in these and kindred investigations."—*How to Work with the Microscope,* third edition, p. 202.

fibres. These may be followed for a considerable distance amongst the developing muscular fibres.

It has been truly stated by Kölliker that the apparently single muscular fibre bearing the swelling is really *a bundle of very fine muscular fibres*, varying from three to seven, or more, in number, and that the apparently *penetrating* nerve-fibres merely pass between these imperfectly developed muscular fibres. I cannot, however, agree with him in the view that the fine muscular fibres result from longitudinal splitting of wider fibres. The bundles of fine muscular fibres under consideration extend, it is true, at a certain period of their development, from one extremity of the muscle to the other; but all the muscular fibres of the bundle do not reach so far. In one bundle sometimes ten or twelve distinct muscular fibres, very closely packed together, may be counted. Near the swelling the muscular fibres are wide, and the fine, tapering, pointed extremities of other young muscular fibres can also be seen. These spindle-shaped muscular fibres are not nearly so long as the ordinary fully developed muscular fibres. In fact, at the swelling, several *spindle-shaped, nucleated,* already *transversely striated* muscular fibres may be observed, and the stages through which the elementary fibres of voluntary muscle pass in their development may be traced.

In these "nerve-tufts" we may indeed study, in the fully-formed animal, striped muscle and nerve in every stage of development. Vessels cannot be traced into the youngest tufts; but in those which consist of several partly grown muscular fibres, capillaries are to be seen; so that the development of muscles, nerves, and vessels can be studied in these imperfectly developed "tufts."

From the above observations, it will be seen that I cannot agree with Kölliker in the view he has taken of these bodies. He says, "Now if it be admitted that the finer muscular fibres composing the bundle are generated by the division of thicker muscular fibres, as Weismann justly concludes, the explanation of the nerve-tufts becomes easy, inasmuch as they may be conceived to arise from *a simultaneous growth and division of the nerve-fibre belonging to the parent muscular fibre, in order that each of the young muscular fibres may obtain its branch of nerve*" (Croonian Lecture, May 1862).

So far from the narrow young muscular fibres *resulting from the division of old ones*, the young muscles and young nerves *are developed from collections of nuclei or masses of germinal matter, precisely resembling those which are found in the embryo.* I believe this to be an invariable law. Many facts make me feel confident that it is quite impossible that *new* textures can be formed by the subdivision of old ones. Formation and development take place upon precisely the same principle in young and old tissues, in health and disease, in simple and complex organisms. New muscular fibres may be developed from old ones in this way:—the "nuclei" may increase in number, the old muscular tissue may *undergo disintegra-*

tion and disappear, in fact the nuclei may live and increase at its expense, and a new mass, consisting entirely of nuclei, or masses of germinal matter, by the agency of which the formed material of the new fibres is at length produced, may result; but never does old tissue split up into new tissue.

As I have pointed out on many occasions, in fully-formed organs there exists a certain proportion of *embryonic germinal matter*, which may undergo development at a future period of life, and if the greater part of this becomes fully-formed tissue, still there remains *embryonic matter for development at a still later period*, and so on. In the situations of these so-called nerve-tufts in the breast-muscle of the frog, new elementary muscular fibres are added to those already formed, and the muscle grows as the frog advances in age. In the formation and growth of the muscular fibres, and in the formation and arrangement of the nerves around them, the movements of the several nuclei or masses of germinal matter to which I have drawn attention, play no unimportant part. (See my paper "On the movements of the living or germinal matter of the tissues of man and the higher animals," Archives, vol. iv. p. 150.)

With reference to the nerves supplying these so-called nerve-tufts, I would remark—

1. That two dark-bordered nerve-fibres, running in the same sheath, may often be traced to one part of the "nerve-tuft."

2. Besides the dark-bordered fibre or fibres, there are invariably very fine fibres running in the same sheath.

3. That the dark-bordered fibres and the accompanying fine fibres divide and subdivide very freely amongst the young muscular fibres, and that thus quite a leash of very fine nerve-fibres results, in the course of which numerous nuclei exist at certain intervals. Many of these can be followed upon or between the muscular fibres, for the distance of the twentieth of an inch or more from the oval swelling. These points are well seen in the figures to which I now direct attention.

4. That the dark-bordered fibre or fibres which enter at the tuft are *not the only* nerve-fibres distributed to these bundles of muscular fibres, but that invariably a bundle, consisting of two or three fine but dark-bordered fibres, is connected with the muscular fibres, at a point above or below that at which the swelling is situated, where the large fibre or fibres enter. Sometimes there are two such bundles, one above and one below. These not unfrequently give off branches, just before they pass to the muscular bundle, which pursue a longer course, and are distributed to other larger muscular fibres; and oftentimes branches pass from one muscular bundle to more distant ones.

From the above observations it follows that these "nerve-tufts" in the breast-muscle of the frog consist of developing muscular fibres, which are freely supplied with nerves; and the number and distribution of the nerves render it probable, not only that there are *entering* and *emerging* fibres, nerve-loops, and plexuses, or networks, upon the muscular fibres, rather

than *free ends*, but that the action of the new muscular fibres may be harmonized with those of the other and older elementary muscular fibres of the muscle by branches of nerve-fibres which are probably commissural.

I will next venture to consider the nature and origin of the nuclei taking part in the development of the muscular nerves; and I would remark that in the frog it is comparatively easy to study the formation of even complex organs out of what used to be called a granular blastema. In each succeeding spring-time not only new ganglion-cells but new ganglia and nerve-fibres, as well as vessels, are developed, and take the place of those which attained their perfect condition in the previous year, but which, having performed their work, have wasted and become converted into mere débris, a great part of which was removed during the period of hybernation.

Now the formation of a new ganglion, of new muscular fibres, of new vessels, and other tissues, and even the formation of elementary organs of complex structure (as I have ascertained specially in the case of the uriniferous tubes of the newt), results from changes taking place in a collection of small spherical masses of germinal matter; and these collections themselves seem to result from the division and subdivision of at most a few masses, all of them of course being the descendants of the original germinal mass formed when impregnation occurred.

Now it may be affirmed most positively, that an entire organ, such as the kidney-tube, or an elementary fibre of muscle, is not formed first and the nerve then spread over it, but the development of the tissue to be influenced proceeds *pari passu* with the development of the nerves which are to influence it. And in the adult animal, where the development of new nerve-fibres takes place, new muscles, &c., are developed in relation with them. I have reason to think, indeed I feel confident, that new nerve-fibres cannot be developed so as to influence an old muscular fibre, or old nerve-fibres caused to influence newly developed muscular tissue; and in the wasting of certain muscles, or other complex tissues, to which nerves are distributed, as may be studied in the frog, all the old tissue seems to be destroyed and removed by the increase of the germinal matter of the respective tissues. Hence it may be stated positively that in every case the new tissue is developed from a mass of "formless blastema"—that is, from a collection of spherical masses of germinal matter which could not be distinguished from the embryonic mass or collection which forms the early condition of every living thing in nature; and in the destruction and removal of every tissue and organ, masses of germinal matter, often resulting from the division of those of the tissue itself, absorb, remove, and in fact live at the expense of, the tissue which is to disappear; and whether this change occurs *physiologically* (that is, as a normal change at certain periods in a healthy and well-developed animal) or *pathologically* (that is, in an organism which has been subjected to the influence of conditions more or less adverse to its well-being), the process is essen-

tially of the same nature; and it would indeed be very difficult to distinguish a collection of spherical masses of germinal matter, from which the tissues of a new being are to be evolved, from a mass of young pus-corpuscles, which may result from the rapid multiplication of masses of germinal matter existing in any tissue of man or the higher animals. In both cases the matter is *formless*; and however much the conclusion may be opposed to the affirmations of great authorities, we are compelled, by a review of the facts ascertained by observation, to infer that there is a far greater difference in the power than there is in the chemical characters, or physical properties, of the matter taking part in these changes.

Many very interesting and highly important facts relating to this inquiry may be obtained from a careful study of the minute changes which occur in the development of the tissues of the imago or perfect insect during the chrysalis stage. So far as I am able to ascertain, the larval tissues and organs are in the first instance completely removed, the germinal matter increases considerably in quantity, and at length a collection of new masses of germinal matter results, which take part in the formation of the new tissues of the developing imago. If those who so confidently affirm that all the phenomena of living beings are physical and chemical would investigate some of these marvellous changes, I venture to think they would very soon withdraw their confident assertions, and admit that the construction of tissues and organs is a process not to be explained by physics and chemistry, or accounted for by any of the known laws of ordinary lifeless matter or force.

I must now advert to a question which I feel incompetent to grapple with, though I cannot permit myself to pass it over. Let me consider if, in the development of new muscular fibres, nerves, and vessels, as occurs in the case of the nerve-tufts of the frog, or in the development of a new ganglion connected with the sympathetic, there are certain masses of germinal matter which, as the direct descendants of pre-existing masses in muscles, nerves, vessels, &c., take part in the development of these tissues respectively, or if they all result from changes occurring in what would be called by some a mass of undifferentiated blastema? In studying the early developmental changes taking place in the embryo, one discovers nothing which would justify the inference that one set of masses is concerned in the development of *all* the future muscles of the body, another of *all* the vessels, another of *all* the nerves, another of all the glandular organs, and so on,—each of these masses or collections being gradually prolonged to distant parts; but it seems rather that the whole is in the first instance formless, and that the process of formation gradually proceeds in many parts at the same time. The brain is not formed first, and other parts of the nervous system extended from this central organ; but the active nervous system, central and peripheral, is developed as a whole, stage succeeding stage, until it attains its fully developed condition in all its parts. If masses of germinal matter for the development of the respective tissues were first formed, and

an extension from each of these to distant parts took place, it must follow that the portion first formed would be the oldest; but all observation seems to show that development gradually goes on in different and distant parts at the same time. And I infer that in the process of regeneration of the lobster's claw, or of the lizard's tail, of the fully formed animal, the several tissues constituting the organs are entirely developed anew from a formless mass, and not by the simple extension of the tissue of the muscles, nerves, vessels, &c., which exist in the stump. In the first instance there results a soft material, which exhibits no indications of definite structure; and as development proceeds, the masses of germinal matter taking part in the development of nerves are seen arranged in lines, and are continuous with those in the nerves of the stump. It is, however, possible that new masses of germinal matter may grow and multiply from these latter and extend into the soft indefinite tissue first produced and destined to serve only a very temporary purpose; but, before I can consider this question advantageously, I must make further observations. And it appears from observations in the case of the frog, that when a new peripheral part or organ is developed, new central nerve-cells are developed in connexion with it. And it is probable (indeed it appears to me certain) that even in man this development of new central and peripheral organs goes on in certain instances. For example, at each pregnancy in the human female, it is probable not only that new muscular fibres, vessels, nerves, &c. are developed in connexion with the growing uterus, but that new *nerve-centres* are also produced, with which the new nerves are connected; and I regard it as most probable that during the development of the lizard's tail and lobster's claw new central nerve-cells in connexion with the new nerve-fibres are developed in the already existing but comparatively simple nerve-centres.

Of the relation of the ultimate branches of the nerve-fibres to the elements of the tissue and to the germinal matter.

In no case does the nerve become continuous with any part of the contractile tissue of muscle; nor is it connected with the nucleus of the muscular fibre or with that of any other tissue.

The ultimate nerve-fibre bears the same relation to the contractile tissue of muscle that it bears to fibres of white fibrous tissue, to cells generally, and to the processes of cells, such as the prolongation from the pigment-cells of the frog, those of the corneal corpuscles in the cornea, &c. The arrangement is such as would lead us to infer that the tissue is influenced by the current passing through the nerve, not by any change involving an anatomical continuity of structure from the nerve to the tissue affected by it, or even in actual contact with any part of it; for in very many instances we can prove that the nerve is not in very close contact with the tissue it influences. Moreover, results resembling those which occur from the action of a nerve may be brought about by the passage of a current of electricity through a wire situated at a considerable distance from the muscle, and

separated from it by non-conducting media; so that, as I have before mentioned, it would seem probable that the varying degrees of muscular contraction are induced by the varying intensity of the current transmitted along a continuous nerve-fibre.

Arguments in favour of the existence of continuous nervous circuits founded upon the structure and arrangement of ganglion-cells.

In a paper already referred to, communicated to the Royal Society in 1864, and published in the 'Transactions,' I endeavoured to show that certain ganglion-cells which had been considered to be apolar or unipolar were invariably connected with at least two nerve-fibres, and that in many cases one of these fibres was coiled spirally round the other, as is well shown in this drawing. These two fibres often appear as one; but not only have I succeeded in demonstrating that they are derived from *different parts of the same cell*, but that they pursue *opposite directions* in the nerve-trunks. I have been led to conclude that all nerve-cells give origin to more than one nerve-fibre, and that these fibres, although they run parallel to one another for a short distance, diverge and pursue very different and indeed opposite courses; and I endeavoured to show that the arrangements I had observed received a ready explanation upon the view of the existence of complete nervous circuits.

In another communication previously referred to, published in the 'Proceedings' of the Royal Society for 1864, entitled "Indications of the paths taken by the nerve-currents as they traverse the caudate nerve-cells," I showed that there existed in the caudate nerve-cells of the spinal cord and medulla oblongata a remarkable series of lines, which passed from each fibre connected with the cell across the body of the cell into every other fibre which diverged from it. I regarded these as indications of the paths taken by the nerve-currents which traversed these cells, and my observations led to the inference that every single cell was the seat of decussation, and therefore formed part of the course, of a vast number of *different nervous circuits*. Upon this view of the constitution of the highly complex central organs of the nervous system, it is not difficult to account for the marvellous number of distinct actions effected, or of the still more wonderful combinations of actions which must occur in the great central organs of the nervous system of man and the higher animals. The axis-cylinder of each dark-bordered nerve-fibre probably forms the common route along which nerve-currents pass from many different parts in the nerve-centre to as many different points in the periphery. Fibres prolonged from several different nerve-cells seem to combine to form one dark-bordered fibre; but these and other points will be readily understood by a cursory examination of the diagrams to which I now direct attention, so that it is unnecessary for me to describe them minutely.

General Conclusions.

To sum up briefly the results of this prolonged inquiry. The first import-

ant point is, that in no tissue have I been able to demonstrate an '*end*' to a nerve. In all cases the nerve-cell or nucleus exhibits fibres proceeding from it in at least *two opposite directions*. The apparent cessation or thinning off of the nerve-fibre in many tissues results from its becoming so thin as to be invisible, unless special methods of investigation are resorted to. It has also been shown that near nervous centres, and near their peripheral distribution, the bundles of nerve-fibres and the individual nerve-fibres divide into very numerous branches. The bundles of coarse or fine fibres given off from a large or small trunk consist of fibres which pursue opposite directions in that trunk, one set passing as it were *from*, the other *towards*, the nervous centre. The nerves distributed to striped muscle of all kinds and to the various forms of unstriped muscle in vertebrata and in invertebrata, are arranged so as to form networks and plexuses, but no indication of terminations or ends is to be seen.

These facts seem to render it probable that the fundamental arrangement of a nervous apparatus is a complete and uninterrupted circuit. This view is supported by the existence of at least two nerve-fibres in all peripheral organs and by facts observed in the branching and division of individual nerve-fibres and of compound nerve-trunks. I have also shown that in nerve-centres it is doubtful if apolar or unipolar cells ever exist. All nerve-cells have at least two fibres proceeding from them in opposite directions, and the multipolar cells in the brain and cord exhibit lines across them which are probable indications of the paths taken by continuous currents which traverse them in many different directions.

The general inference from this anatomical inquiry is, that a current probably of electricity is constantly passing through all nerve-fibres, and that the adjacent tissues are influenced by the varying intensity of this nerve-current rather than by its complete interruption and reestablishment; so far as I know, no fact has ever been discovered which would justify the conclusion that there exists any arrangement for making and breaking contact in any part of the nervous system. In all cases it is probable that every nervous circuit is complete, and that there is no interruption of the structural continuity of a nerve-fibre at any part of its course.

May 18, 1865.

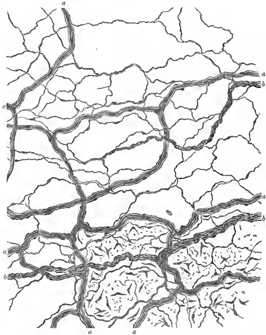
Major-General SABINE, President, in the Chair.

His Royal Highness Louis Philippe of Orleans, Count of Paris, was admitted into the Society.

The following communications were read:—

I. "On Newton's Rule for the Discovery of Imaginary Roots of Equations." By J. J. SYLVESTER, F.R.S. Received May 4, 1865.

In the first part of my "Trilogy of Algebraical Researches," printed in



Connective tissue covering part of the mylohyoid muscle of the frog, and extending from its posterior portion. *a*. Capillary vessels, with their nerve-fibres. *b*. Bundles of fine dark-bordered nerve-fibres, from which fine nerve-fibres may be traced to the capillaries, and to their distribution in the connective tissue, where they form networks of exceedingly fine compound fibres. The engraving represents the specimen as magnified only 110 diameters; but the original drawing was taken from it when magnified by a much higher power.